# AdvaMed Comments

| Date | Document |
|---|---|
| December 3, 2002 | **Medical Devices Made With Polyvinylchloride (PVC) Using the Plasticizer di-(2-Ethylhexyl)phthalate (DEHP); Draft Guidance for Industry and FDA** |

| | Commenter | Line No. | Proposed Change | Comment/ Rationale |
|---|---|---|---|---|
| 1. | AdvaMed | 23 | Remove words "or eliminate" | Cannot "eliminate" risk – only reduce. |
| 2. | AdvaMed | 24-25 | Change to read "**potential** risks that may be associated with DEHP. We are suggesting that you label certain devices **to indicate DEHP presence** and consider..." | Must clearly indicate that the risk(s) from DEHP exposure in humans is only hypothetical (e.g., see line 31). In addition, the proposed labelling discussed throughout this document is simply to indicate content, not to specify levels, as the current wording in lines 24-25 would suggest. |
| 3. | AdvaMed | 33 | Change to read, "exceed **hypothetical tolerable intake levels FDA calculated using data from the rodent studies**". | Currently, there is no level identified in any research article or risk assessment (including FDA's) above which adverse effects in humans would definitely occur. The tolerable intake (TI) levels calculated in FDA's risk assessment are again, hypothetical levels based on animal studies, and no human data exist to corroborate the assumptions (see line 31 in the draft, which clearly states "no human studies that show such effects"). |
| 4. | AdvaMed | 31-33 | Remove sentence Line 31-33. | Sentence regarding "...exposure to DEHP could exceed the levels that are not expected to cause adverse health effects..." does not make sense. Have already made it clear in Line 30 that toxic and carcinogenic effects of DEHP have not been demonstrated in human studies. |
| 5. | AdvaMed | 39 | Add clarification to sentence as:<br><br>...devices where PVC containing DEHP may release some DEHP in certain conditions when in contact... | The content of DEHP is not the issue, but the leachable release of DEHP. |
| 6. | AdvaMed | 50 | Remove "contain" and replace with "release." | The content of DEHP is not the issue, but the leachable release of DEHP. |
| 7. | AdvaMed | 54 | Specify as IV administration **of lipids or blood products in the NICU** | Document should remain focused on "small subset of devices" (see lines 38-39) and potential exposure scenarios identified as "sensitive populations" (lines 50-51) |
| 8. | AdvaMed | 55 | Delete completely | Too few hemodialysis procedures in neonates or pregnant women (these are the sensitive patient populations addressed in FDA's risk assessment) to warrant labelling all dialysis tubing. |
| 9. | AdvaMed | 56 | Insert after ECMO, "**in NICU applications.**" | Document should remain focused on "small subset of devices" (see lines 38-39) and potential exposure scenarios identified as "sensitive populations" (lines 50-51) |
| 10 | AdvaMed | 57 | Specify as cardio-pulmonary bypass (CPB) procedures **in NICU applications** | Document should remain focused on "small subset of devices" (see lines 38-39) and potential exposure scenarios identified as "sensitive populations" (lines 50-51) |

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| 11 | AdvaMed | 60 | Delete completely | Industry already uses non-PVC containers for TPN solutions and has for many years. |
| 12 | AdvaMed | 65 | Change to read "What does FDA recommend that you do if a device in the category(ies) cited above is made with PVC containing DEHP" | Document should remain focused on "small subset of devices" (see lines 38-39) and potential exposure scenarios identified as "sensitive populations" (lines 50-51) |
| 13 | AdvaMed | 68-74 | Rewrite as follows (changes are indicated in bold):<br><br>We encourage you to consider all mechanisms to reduce exposure to DEHP in **potentially sensitive patient populations e.g., neonates.** Specifically we recommend that you consider the feasibility of replacing PVC containing DEHP with either alternative materials or plasticizers, or using coatings that may minimize patient exposure to DEHP **in certain medical devices.** An additional design requirement should be considered for the small subset of medical devices where PVC containing DEHP may come in contact with the tissue of a sensitive patient population in a manner and for a period of time that may raise concerns about the aggregate exposure to DEHP. | FDA's recommendation is too broad in light of conclusions of the FDA safety report and other statements in the draft guidance. The FDA safety report concluded that for the vast majority of medical device uses, DEHP poses "little or no risk" to patients. In line 38 of the draft guidance, FDA acknowledges that their concern is on the "small subset of medical devices where PVC containing DEHP may come in contact with the tissue of a sensitive patient population in a manner and for a period of time that may raise concerns about the aggregate exposure to DEHP." We believe that many devices used in Neonatal Intensive Care units (NICUs) meet this criteria and should be a primary focus." As written, the recommendation for manufacturers to consider "minimizing patient exposure to DEHP" as a design requirement in their design control procedures appears to apply to all medical devices. It should only apply to medical devices that are clearly intended for use in the potentially sensitive patient population, e.g., neonates. |
| 14 | AdvaMed | 84 | Insert sentence at the end to read, "Importantly, as with any material change (PVC or other), the standard approach to evaluating biocompatibility using ISO 10993-1 criteria should be applied". | This is a significant gap in the current draft. As it currently reads, the impression is that substitution of virtually any material other than PVC would inherently make a device "safer". This is not the case, and any/all materials should undergo appropriate evaluations as outlined in existing regulatory guidance FDA follows (i.e., ISO 10993 as described in the G-95 Blue Book Memorandum). |
| 15 | AdvaMed | 76-109 | | The language in the draft FDA guidance suggests that manufacturers may be able to make material changes in their products without the standard regulatory review. Nonetheless, it is important that manufacturers evaluate new or modified products through verification and validation studies to assure that the products meet safety and performance requirements. We believe that these testing standards, as well as regulatory review, are particularly important when considering materials that do not have prior experience or characterization in the medical field. We agree with FDA's implication that manufacturers should consider submissions if a new material's suitability is not established for a particular use. |

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| 16 | AdvaMed | 111-119 | Rewrite as follows (changes are indicated with strike-outs and bolded text):<br><br>What if I choose not to change the material in my device? ~~Should I revise the labelling to state the device contains DEHP?~~ **Should I disclose DEHP content?**<br>Yes, we recommend that you ~~clearly indicate through user labelling that your device contains DEHP.~~ **provide information to clinicians regarding the presence of leachable DEHP in your devices. You can do this through your product promotional materials or by means of the product labelling. You can choose to identify only those products that are non-DEHP or those that contain leachable DEHP.** Although at this time, FDA believes there is insufficient information to justify requiring device manufacturers to disclose the presence of this chemical **in their products**, ~~in the device's labeling~~, there is considerable interest among some consumers and practitioners in mitigating any risks that exposure to DEHP may present.. | We agree that a manufacturer's disclosure of the DEHP content of medical devices can assist healthcare practitioners in making informed decisions regarding patient care. However, we believe that a flexible approach to the methods for such disclosure is warranted. A manufacturer may choose to provide a list of non-DEHP products in their product catalogue or to include a statement of non-DEHP or DEHP content in the product labelling. These alternative approaches would provide the information needed to address customers' questions on whether the device contains DEHP. |